

Product Performance Data Evaluation Report
Kevin J. Sweeney, Entomologist
Insecticide Branch
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EPA Reg. No./Flie Symbol: 62719-ULG & ULU

Product Names: IG-007 & AG-007

Registrant: Dow AgroSciences Inc.

Reviewer: Joseph Tavano

Product Manager: Marion Johnson, PM 10

Submission: S614951, S614952

DP: D285934, D284936

Active Ingredient: 0.5% noviflumuron

Application Rates: 0.5% delivered via in-ground and above ground bait devices as in the Sentricon system

Pests: All economically important subterranean termite species in the United States.

Sites: Outdoor and indoor residential and commercial areas. Non-food use.

OPPTS Guideline: none.

These products are the section 3 registrations for the new chemical noviflumuron. The registrant submitted laboratory and field studies. In addition, these products are being tested in an EUP program. I reviewed the three submitted studies for the section 3 together with the other studies that were submitted to support the EUP. I stated my recommendations for the section 3 registration.

Submitted with the Section 3 registration application:

MRID 45516724 Kinetics of Uptake, Clearance, Transfer, and Metabolism of Hexaflumuron and XR-007 in Termites (*Reticulitermes flavipes*) by J.J. Sheets.

MRID 45516725 Uptake Rate of Carbon-14 Hexaflumuron Force Fed to Groups of *Reticulitermes flavipes* by J.J. Sheets.

MRID 45516726 Results of Field Trials Conducted in the U.S. from 1998-2000 to Compare the Effectiveness of XDE-007 and Hexaflumuron as Bait Toxicants for Control of Subterranean Termites by R.J. Sbragia et al.

Submitted with the EUPs for noviflumuron

MRID 45262204 The Performance of XDE-007 in Above Ground and In-Ground Subterranean Termite Trials Conducted in Northern California and Hawaii During 1998 by R.J. Sbragia.

MRID 45232423 Field determination of the Concentration Acceptance of Hexaflumuron and XDE-007 to Subterranean termites (*Reticulitermes* spp.) 1997-1998 by J.J. DeMark

MRID 45262202 Response of Field Colonies of *Coptotermes actinaciformis* (in Australia) to the Bait Toxins XR-007 and Hexaflumuron by M. Lenz.

MRID 45262203 Response of Field Colonies of *Coptotermes lacteus* to the Bait Toxins XR-007 and Hexaflumuron by P.V. Gleeson

MRID 45262201 Response of Field Colonies of *Coptotermes acinaciformis* to the Bait Toxicant XR-007 and Hexaflumuron, Australia 1997 by W.J. Lucas.

No MRID Assigned: XDE-007 Termite Bait Experimental Use Proposal - A technical Overview and Comparison to Hexaflumuron by K.S. Gilbert, DAS. September 2000.

Reviews of Submitted Studies:

MRID 45516724 Kinetics of Uptake, Clearance, Transfer, and Metabolism of Hexaflumuron and XR-007 in Termites (*Reticulitermes flavipes*) by J.J. Sheets. 1999.

This was a non-GLP laboratory study conducted during development of noviflumuron as a termite bait insecticide.

Noviflumuron (XR-007) is a fluorinated benzylphenyl urea that affects/inhibit chitin synthesis in animals with exoskeletons (Arthropoda etc.). The exact mode of action is not understood because there are no *in vitro* methods available to assay effects on enzyme activity. Presumably, this insecticide inhibits chitin synthesis when insects molt during growth or metamorphosis, thereby preventing proper formation of a new exoskeleton. Noviflumuron is closely related - in terms of chemical properties, structure, and activity - to the EPA registered termite bait insecticide, hexaflumuron. The subject study compares the "activity" of noviflumuron and hexaflumuron in the worker caste of the Eastern Subterranean termite, *Reticulitermes flavipes*. The author presents data showing that noviflumuron kills termites faster

than hexaflumuron at the same dose (ng/termite). The reason for this result is not known, but based on data that show. Neither noviflumuron or hexaflumuron appear to be metabolized by the termite, however, hexaflumuron is excreted more quickly. Noviflumuron is more stable and is distributed throughout the termite in a short time period in comparison to hexaflumuron.

Termites in this study were "forced fed" both noviflumuron and hexaflumuron in no-choice assays. The tested concentrations were 0.1% and 0.5% of the respective active ingredient. Noviflumuron and hexaflumuron were "labeled" with the radioactive isotope carbon-14. The uptake, transfer (including trophallaxis), and clearance of the parent compound in termites was based on the measurement of carbon-14 radioactivity. Only live termites were assayed. Dead termites could not be assayed. Thin layer chromatography was used as a qualitative tool to indicate the degree of metabolism of either noviflumuron or hexaflumuron in the termite. The extracts from treated termites were visually similar to those of the laboratory standards.

The 0.5% concentration of noviflumuron resulted in about 30% faster termite uptake, leading to feeding cessation and greater than 80% mortality in 25 days vs. 35 days for the 0.1% concentration as measured by population elimination in the laboratory assays. However, the statistical analyses did not reveal significant differences in the consumption, clearance rate, half-life, and time to "colony elimination" at $p < 0.1$. The rate of clearance and the half-life inside the termite were significantly different at $p < 0.1$ (90% confidence interval). Noviflumuron clearance (29 days) is four-fold slower than that of hexaflumuron (8 days) at the same dilution. Therefore, the half-life inside the termite is four times greater for noviflumuron when compared to hexaflumuron. This result may be attributed to the increased binding in termite tissues due to the increased electronegativity resulting from the fluorination of the terminal carbon atom.

The author theorized that the longer half-life of noviflumuron in the termite may improve its chitin synthesis inhibition abilities (presumably by binding more tightly to the chitin synthetase enzyme(s) and efficacy against a wider range of target arthropods. The slow rate of clearance results in wider distribution of the molecule within the termite leading to faster mortality at a lower internal concentration. Theoretically, the long half-life and retention of noviflumuron within a termite population could ultimately improve secondary kill and lead to death of the primary reproductive termites. However, such claims need to be supported by field studies with native termite populations.

MRID 45516725 Uptake Rate of Carbon-14 Hexaflumuron Force Fed to Groups of *Reticulitermes flavipes* by J.J. Sheets. 1997.

This was a non-GLP laboratory study to determine the amount and rate of uptake of hexaflumuron in the worker caste of the Eastern Subterranean termite, *Reticulitermes flavipes*. The study also examined and compared two different techniques of assaying for carbon-14 labeled hexaflumuron. The DAS method was compared with that of Clement. DAS theorized that hexaflumuron uptake was underestimated by Clements because it was not released from bound proteins within the termite, thus "quenching" the C-14 signal. DAS digested the termites in the

scintillation vials. Digestion with Protosol under hot alkaline conditions made greater quantities of labeled hexaflumuron available, increasing radioactive recovery during the quantitative analysis, scintillation counting for labeled carbon-14.

This study did examine transfer, distribution or excretion of hexaflumuron. Uptake increased with increased hexaflumuron concentration. More treated cellulose and hexaflumuron were ingested at 0.5% compared to 0.1%. Repellency at either concentration was not reported.